Infectious Diseases

COST-EFFECTIVENESS OF NEWER TREATMENT STRATEGIES FOR INFLUENZA

Smith KJ, Roberts MS. *Am J Med.* 2002;113:300–307

Purpose of the Study. Recent advances in the diagnosis and treatment of influenza, such as rapid testing and neuraminidase inhibitor therapy, are available, but their place in clinical practice and their cost-effectiveness have not been determined.

Patient Population and Methods. To estimate the cost-effectiveness of these newer interventions, we used a decision model that compared several influenza management strategies: no testing or treatment, amantadine or rimantadine treatment without testing, testing then amantadine or rimantadine treatment, neuraminidase inhibitor treatment without testing, or testing then neuraminidase inhibitor treatment. Antiviral therapy began within 48 hours in febrile patients with characteristic symptoms of influenza. We assumed that antiviral treatment did not change rates of influenza complication or mortality, and chose parameter values in the baseline analysis to bias slightly against antiviral treatment and toward testing strategies.

Results. In the baseline analysis, testing strategies are more expensive and less effective than treatment strategies. Amantadine costs $9.06 per illness day avoided or $11.60 per quality-adjusted day gained. Compared with amantadine, zanamivir costs $198 per illness day avoided or $185 per quality-adjusted day gained, whereas oseltamivir costs $252 per illness day avoided or $235 per quality-adjusted day gained. In elderly patients who require reduced dosage, rimantadine costs $128 per quality-adjusted day gained compared with amantadine. In younger patients, amantadine is favored if the likelihood of influenza A is >67%; otherwise, neuraminidase inhibitors are favored. Testing strategies are more costly and less effective when the influenza probability is >30%. No testing or treatment is favored if the influenza probability is <32% and the influenza utility is >0.77. In elderly patients, amantadine is favored over rimantadine if the utility of medication side effects is >0.94.

Conclusions. Antiviral treatment of influenza without rapid testing is reasonable economically in febrile patients with typical symptoms during influenza season. The choice of antiviral agent depends on age, the likelihood of influenza A, and the willingness to pay per quality-adjusted day gained.

Reviewer's Comments. I found this analysis to be very interesting, in part because I agreed with the conclusions. In my experience, the ability to use these agents is limited and their effectiveness (even when taken before exposure) is of marginal benefit. Amantadine and rimantadine are generally effective, but only against influenza A. Side effects occur more commonly when taking antihistamines or anticholinergics. The neraminidase inhibitors are effective against A and B strains but are expensive, and zanamivir should not be used in patients with asthma. Usually by the time a patient presents with typical symptoms and you've managed to convince their insurance plan to cover the cost of the medication, it's too late to treat. Patients would have been better off had they listened to their mothers when they told them: "Get a flu shot, Mister Big Shot!"

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SAFETY OF THE TRIVALENT, COLD-ADAPTED INFLUENZA VACCINE IN PRESCHOOL-AGED CHILDREN

Piedra PA, Yan L, Kotloff K, et al. *Pediatrics.* 2002;110: 662–672

Purpose of the Study. Influenza is a major cause of morbidity in all age groups. The study objective was to provide safety data for the intranasally administered, trivalent, cold-adapted influenza vaccine (CAIV-T) in young children using a multicenter, prospective, randomized, double-blind, placebo-controlled study.

Study Population. Healthy children 15 to 71 months old were enrolled. Exclusion criteria included history of significant hypersensitivity to eggs or a chronic illness for which trivalent inactivated influenza virus (IIV-T) would be recommended. Inclusion in years 2 to 4 of the study required inclusion in all of the previous consecutive years beginning in 1996.

Methods. Each year CAIV-T provided by Aviron (Mountain View, CA) contained vaccine strains that matched antigens consistent with the licensed US Food and Drug Administration IIV-T product. In year 1, 1314 children were enrolled in the 2-dose cohort (either active CAIV-T or placebo) and 288 were enrolled in the 1-dose cohort. In year 2, 1358 original participants received 1 dose of CAIV-T or placebo to match their original treatment. In years 3 and 4, 642 and 549 children, respectively, received their third and fourth doses of CAIV-T in an open-label extension. Safety was evaluated by measuring the occurrence of specific or unexpected symptoms within 10 days of vaccination, incidence of an acute illness and use of medication within 11 to 42 days of vaccination, and occurrence of a serious adverse event within 42 days of vaccination.

Results. In the first year, runny nose or nasal congestion, vomiting, muscle aches, and fever were significantly associated with the first dose of CAIV-T. Runny nose was the only symptom associated with CAIV-T after the second dose. In years 2 to 4 specific symptoms were not associated with CAIV-T. The symptoms associated with CAIV-T were most likely to occur on day 2, after the first dose of vaccine. Vomiting, abdominal pain, and muscle aches were associated with the first dose of vaccine. Unexpected symptoms most commonly involved the gastrointestinal system. A significant increase in the use of analgesics/antipyretics was observed with the first dose of CAIV-T compared with placebo (23.5% vs 16.6%). CAIV-T was not associated with illness or medication use on days 11 to 42 or serious adverse events.

Conclusions. CAIV-T was deemed safe in preschool-aged children. Mild respiratory, gastrointestinal, and systemic symptoms were observed primarily with the first dose of vaccine and occurred in a minority of children. Subsequent consecutive annual doses of CAIV-T were tolerated without significant effects.

Reviewer's Comments. Influenza remains a significant cause of morbidity in children. The American Academy of Pediatrics (AAP) has recommended vaccinating all children between 6 and 23 months of age using the IIV-T product, especially those at high-risk of hospitalization. Nonetheless, most children are still not immunized, perhaps because of a lack of desire to use the injectable product. This study demonstrates that the CAIV-T is safe with minimal side effects in healthy children. Hopefully, we will see this vaccine come to market in the near future.

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SAFETY OF THE TRIVALENT, COLD-ADAPTED INFLUENZA VACCINE IN PRESCHOOL-AGED CHILDREN

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